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10/538,226	06/06/2005	Marnix L Bosch	NWBI135357	9406

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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/538,226	BOSCH, MARNIX L	
	Examiner	Art Unit	
	STEPHEN RAWLINGS	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20101210*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed February 9, 2011, is acknowledged and has been entered.

2. Claims 1-32 are pending in the application and are currently under prosecution.

Election/Restriction

3. Claims 10-12, although "withdrawn" by the preceding Office action, are not presently withdrawn because the claims are directed to the elected species of invention, albeit in the alternative. Moreover, claims 10-12 merely recite limitations upon a non-elected species of invention and do not recite limitations upon the elected species of invention.

4. The requirement to elect a species of the invention wherein the composition according to claim 21 comprises partially mature dendritic cells demonstrating an up-regulation of one or more of the co-stimulatory molecules selected form CD80, CD86, and CD54 is withdrawn in favor of rejoinder of said subject matter.

Information Disclosure Statement

5. The information disclosure filed December 10, 2010, has been considered. An initialed copy is enclosed.

Notably, the disclosure statement lists a search report. The listing of the references cited in the search report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS

must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the search report have not been considered unless the references are also listed in the IDS (and have not been crossed-through). Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

Response to Arguments

6. Applicant's arguments with respect to the rejection of the claims on the grounds set forth in the preceding Office action mailed August 9, 2010, have been considered but are moot in view of the new grounds of rejection.

Priority

7. Applicant's claim under 35 U.S.C. §§ 119(e) and/or 120, 121, or 365(c) for benefit of the earlier filing date of PCT Application No. PCT/Us03/38672, filed December 5, 2003, which claims benefit of U.S. Provisional Application No. 60/431,267, filed December 6, 2002, is acknowledged.

However, claims 1-32 do not properly benefit under §§ 119 and/or 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under §§ 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of

35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). See M.P.E.P. § 201.11.

In addition, some of the claims do not properly benefit from the earlier filing date of U.S. Provisional Application No. 60/431,267 because this document fails to provide written support for the subject matter to which the claims are directed. In particular, it is noted that the with regard to claims 6 and 10-12, the provisional application fails to provide written support for the claimed method in which the maturation agent is, for example, an imidazoquinoline compound or an agonist of a Toll-like receptor (TLR). Then, with regard to claim 22, it is further noted that the provisional application fails to describe the composition in which the mature dendritic cells demonstrate an up-regulation of CD54.

Accordingly, the effective filing date of the claims is deemed the filing date of the international application, namely December 5, 2003.

Claim Objections

8. Claims 6 and 101-12 are objected to as being drawn in the alternative to the subject matter of a non-elected species of the invention.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-32 are indefinite for the following reasons:

In accordance with a recent decision by the Federal Circuit (*Halliburton Energy Services Inc. v. M-I LLC*, 85 USPQ2d 1654, 1658 (Fed. Cir. 2008)):

> 35 U.S.C. § 112, ¶ 2 requires that the specification of a patent "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which

> the applicant regards as his invention." Because claims delineate the patentee's right to exclude, the patent statute requires that the scope of the claims be sufficiently definite to inform the public of the bounds of the protected invention, i.e., what subject matter is covered by the exclusive rights of the patent. Otherwise, competitors cannot avoid infringement, defeating the public notice function of patent claims. Athletic Alternatives, Inc. v. Prince Mfg., Inc., 73 F.3d 1573, 1581 (Fed. Cir. 1996) ("[T]he primary purpose of the requirement is 'to guard against unreasonable advantages to the patentee and disadvantages to others arising from uncertainty as to their [respective] rights.'") (quoting Gen. Elec. Co. v. Wabash Appliance Corp., 304 U.S. 364, 369, (1938)). The Supreme Court has stated that "[t]he statutory requirement of particularity and distinctness in claims is met only when [the claims] clearly distinguish what is claimed from what went before in the art and clearly circumscribe what is foreclosed from future enterprise." United Carbon Co. v. Binney & Smith Co., 317 U.S. 228, 236 (1942).

Claims 1-32 are directed to a composition comprising "partially mature dendritic cells", but it cannot be ascertained whether any given dendritic cell, which is not "immature" or "mature", should be considered "partially mature". As Applicant should be aware the maturation of a dendritic cell is a very complex process, which perhaps occurs in degrees or increments. As a population of precursors to the dendritic cell differentiates upon stimulation by appropriate agents, individual cells within the population undergo a series of sometimes incomplete, sometimes overlapping phenotypic changes, which are typically characterized by the expression of certain marker proteins at the surface of the cells, as well as by their morphologies. Notably the specification does not clearly define the features that characterize the claimed "partially mature dendritic cells" but instead provides factual evidence suggesting that those features might vary rather substantially depending upon their origins and the means by which their precursors are induced to undergo maturation[1]. As such it is submitted to be a very difficult, if not impossible, feat to envision, identify and/or recognize a composition comprising "partially mature dendritic cells", where it is not

[1] See, e.g., Tables 2 and 3 at pages 19 and 20 of the specification, which include data indicating that dendritic cells induced to undergo maturation using different agents or combinations thereof display different phenotypes characterized by varying expression of cell surface markers. For example, according to Table 2, 28.1% of a population of untreated immature dendritic cells expresses CD86. After treatment with R848 there is a small (likely insignificant) increase in the number of cells expressing this marker (31.3%), but after treatment with a combination of BCG and interferon, for example, there is a more sizeable increase in the percentage of cells in the population expressing CD86 (66%). Such data indicate the particular features that might be used to identify the claimed "partially matured dendritic cells" will be expected to vary considerably depending upon the means by which the cells are induced to undergo maturation.

known how such cells are necessarily characterized. When is a dendritic cell no longer considered "immature" but "partially mature"? When is a dendritic cell considered "partially mature" but not yet "mature"? Since the answers to these questions are not found in the specification it is apparent that the claims cannot be unambiguously construed; and for these reasons, it is submitted that the claims fail to delineate the metes and bounds of the subject matter that is regarded as the invention with the requisite clarity and particularity to permit the skilled artisan to know or determine infringing subject matter, so as to satisfy the requirements set forth under 35 U.S.C. § 112, second paragraph.

Applicant is duly reminded that with regard to § 112, second paragraph, M.P.E.P. § 2171 states that there are two separate requirements set forth in this paragraph: the claims must set forth the subject matter that applicants regard as their invention; and the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

With regard to the first requirement, M.P.E.P. § 2171 states the determination of the sufficiency of the claim to satisfy that requirement is subjective because it is dependent on what the applicant for a patent regards as the invention; as such, it is apparent that no amount of reference to the "conventional art cited in the specification" should permit the artisan to know that which is held in the mind of the applicant.

Then, as that is the case, it is important to note instances in which Applicant's remarks suggest that their invention is something other that which is claimed.

Indeed, since, for example, most artisans consider CD83 to be a marker of "mature" dendritic cells[2], it is importantly noted that according to the disclosure the "partially matured dendritic cell" may or may not express this marker[3].

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[2] See, e.g., Zhou et al. (*Proc. Natl. Acad. Sci. U S A.* 1996 Mar 19; **93** (6): 2588-92). Interesting, while CD83 may be a marker used to identify "mature" dendritic cells, Zhou et al. teaches that not all mature dendritic cells express CD83. Apparently there are "mature" dendritic cells arising from myelomonocytic cells, which do not express CD83 even after culture or activation (see page 2588). Thus, although a dendritic cell expressing CD83 might be considered "mature" the lack of expression of CD83 by a dendritic cell may not indicate the cell is not "mature". Such disclosures support the position taken here that the claims fail to reasonably apprise the skilled artisan of the metes and bounds of the subject matter that is regarded as the invention since the features that might be used to define the different stages of maturation of dendritic cells are blurred and indefinite.

Notably, despite such considerations, it appears that Applicant has previously traversed the propriety of maintaining similar grounds of rejection arguing that the claims are not indefinite because the specification teaches certain features of Applicant's invention, which are not recited in the rejected claims, but remarking that the claims of an application are read in view of the specification; and in response to such arguments, Applicant has been reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

To further address the manner in which the claims are to be read in light of the specification in determining whether the claims satisfy the requirement set forth under § 112, second paragraph, M.P.E.P. § 2106 (II) states:

> USPTO personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). **Limitations appearing in the specification but not recited in the claim should not be read into the claim**. *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in view of the specification" **without importing limitations from the specification into the claims unnecessarily**). *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 551 (CCPA 1969). See also *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) ("During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow.... The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed.... An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.") (Emboldened added for emphasis).

M.P.E.P. § 2106 (II) continues:

> While it is appropriate to use the specification to determine what applicant intends a term to mean, **a positive limitation from the specification cannot be read into a claim that does not itself impose that limitation**. A broad interpretation of a claim by USPTO personnel will reduce the possibility that the claim, when issued, will be interpreted more broadly than is justified or intended. An applicant can always amend a claim during prosecution to better reflect the intended scope of the claim.
>
> Finally, when evaluating the scope of a claim, every limitation in the claim must be considered. USPTO personnel may not dissect a claimed invention into discrete elements and then evaluate the elements in isolation. Instead, **the claim as a whole must be considered**. See, e.g., *Diamond v. Diehr*, 450 U.S. 175, 188-89, 209 USPQ 1, 9 (1981).

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[3] See, e.g., the disclosure at paragraph [0030] of the published application (U.S. Patent Application Publication No. 20060057120-A1).

Accordingly, rather than requiring that the claims are insolubly ambiguous, the Board of Patent Appeals and Interferences has stated in a rare precedential opinion that the "USPTO is justified in using a lower threshold showing of ambiguity to support a finding of indefiniteness under 35 U.S.C. § 112, second paragraph, because the applicant has an opportunity and a duty to amend the claims during prosecution to more clearly and precisely define the metes and bounds of the claimed invention and to more clearly and precisely put the public on notice of the scope of the patent." *Ex parte Miyazaki*, Appeal 2007-3300, November 19, 2008, at p. 12.

Additionally, with regard to the first requirement set forth under § 112, second paragraph, M.P.E.P. § 2171 states the determination of the sufficiency of the claim to satisfy that requirement is subjective because it is dependent on what the applicant for a patent regards as the invention.

As that is the case, it is important to note instances in which Applicant's remarks suggest that their invention is something other that which is claimed. Here, again, since it appears that Applicant has previously traversed the propriety of maintaining similar grounds of rejection arguing that the claims are not indefinite because the specification teaches certain features of Applicant's invention, because many of the features relied upon by Applicant are not recited in the rejected claims, such arguments suggest the subject matter that is regarded as the invention is something other that which is claimed.

With further regard to the first requirement set forth under § 112, second paragraph, M.P.E.P. § 2171 states the determination of the sufficiency of the claim to satisfy that requirement is subjective because it is dependent on what the applicant for a patent regards as the invention. As that is the case, it is important to note instances in which Applicant's remarks suggest that their invention is something other that which is claimed because such remarks constitute evidence that shows that a claim does not correspond in scope with that which applicant regards as applicant's invention[4]. Furthermore, M.P.E.P. § 2173 states that a clear measure of what an applicant regards

as the invention is necessary so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention. This is particularly important here since one cannot make and/or use the claimed compositions and processes without knowing how "partially matured dendritic cells" are necessarily identified and isolated.

Notably Applicant has previously traversed the propriety of maintaining similar grounds of rejection arguing that the claims are not indefinite because the skilled artisan would understand that the claimed "partially matured dendritic cells" are dendritic cells that are not either "immature" or "mature" but which have characteristics intermediate to either of these states[5]; yet it cannot be understood how, for example, it might be ascertained how a dendritic cell, which has only begun to undergo the process of maturation, but which has not matured, might be identified. This is particularly problematic since it appears that the features that identify the "immature" and "mature" dendritic cells are indefinite as well.

Finally, with further regard to the second requirement, M.P.E.P. § 2173 states "[in] reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent".

In this instance, it is submitted that the claims fail to satisfy the requirements set forth under 35 U.S.C. § 112, second paragraph, that require that the claims clearly and particularly point out the subject matter that is regarded as the invention because it cannot be ascertained when any given dendritic cell should be considered "partially matured".

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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[4] See M.P.E.P. § 2172 (II).

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereinafter "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

These guidelines state that rejection of a claim for lack of written description, where the claim recites the language of an original claim should be rare. Nevertheless, these guidelines further state, "the issue of a lack of written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant has possession of the claimed invention" (*Id.* at 1105). The "Guidelines" continue:

> The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art. This problem may arise where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process.

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[5] See, e.g., page 16 and 17 of the response filed February 9, 2011.

With further regard to the proposition that, as *original* claims, the claims themselves provide *in haec verba* support sufficient to satisfy the written description requirement, the Federal Circuit has explained that *in ipsis verbis* support for the claims in the specification does not *per se* establish compliance with the written description requirement:

> Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). *See also:* University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 1892 (CA FC 2004).

Thus, an original claim may provide written description for itself, but it must still be an adequate written description, *which establishes that the inventor was in possession of the invention.*

In this instance, the claims are directed to a composition comprising "partially matured dendritic cells" or to a process of using such a composition to produce an anti-tumor immune response.

As explained in the above rejection of the claims under 35 U.S.C. § 112, second paragraph, the particular features that characterize the claimed "partially matured dendritic cells", which might permit the skilled artisan to immediately envision, recognize or isolate such cells, are not claimed and are not clearly (and without ambiguity) described in this application.

Applicant is reminded that "generalized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

In this instance, there is no language that adequately describes with the requisite clarity and particularity the claimed "partially matured dendritic cells", which must be used to make and/or use the claimed invention so as to achieve the claimed objectives.

Although the claimed cells must be effective to produce an anti-tumor immune response in an individual, a description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

As discussed in the above rejection, the specification discloses that the characteristics of the claimed "partially matured dendritic cells" can vary rather substantially depending upon their origin and the maturation agent that is used to initiate their maturation. Thus, the specification supports the position taken here in that the claims fail to reasonably correspond to the subject matter that is described with due clarity and particularity by the disclosure, so as to satisfy the written description requirement set forth under 35 U.S.C. § 112, first paragraph. This is because it cannot be ascertained whether or not any given dendritic cell should be considered "partially matured" because the features that characterize such cells are not described in this application with any of the requisite clarity and particularity necessary to permit the skilled artisan to know or determine the identity of the cells.

Turning to a slightly different issue, the claims are directed to "partially matured dendritic cells", which have been induced to initiate maturation by contact with a "maturation agent". Although the specification describes a few of such compounds that have been used the claims are not so limited and none of the particularly described compounds, which are suitably used in the practice of the claimed invention to induce the differentiation and maturation of dendritic cell precursor cells or immature dendritic cells, are reasonably deemed adequately representative of the genus as a whole since its members are composed of markedly different materials and/or have such widely varying structures.

While the written description requirement can by satisfied without an actual reduction to practice, the disclosure of a catalog of potentially effective substances that might be found to be useful in practicing the claimed invention does not fulfill the written description requirement. Recognizing that the claims are drawn to a method comprising administering to an individual a composition comprising "partially matured dendritic cells", which have been induced to undergo maturation by exposure to any of a plurality of materially and structurally disparate "maturation agents", it is aptly noted that the

Federal Circuit has decided that a generic statement that defines a genus of substances by *only* their functional activity, i.e., the ability to initiate maturation of dendritic cells, does not provide an adequate written description of the genus. See *The Reagents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997). The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

Although *Lilly* related to claims drawn to genetic material, the statute applies to all types of inventions. "Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1894 (CAFC 2004). The claimed method depends upon finding a compound that has the ability to induce the partial maturation of dendritic cells; without such a compound, it is impossible to practice the invention.

In addition, although the skilled artisan could potentially identify agents that might be used in practicing the claimed invention by screening for substances that are capable of inducing the partial maturation of dendritic cells, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.*

> The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

Absent the adequate description of a representative number of members of the genus of maturation agents to which the claims are directed, the supporting disclosure amounts to no more than a mere invitation to identify a substance that can be used as a maturation agent for inducing the partial maturation of dendritic cells.

Finally, Guidelines states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). "Guidelines" further states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Moreover, because the claims encompass a genus of substances having the ability to induce the partial maturation of dendritic cells, which vary materially and structurally, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. In this instance, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; Applicant has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; and Applicant has not described distinguishing identifying characteristics

sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

In this case, since the claims are so broad, and the disclosure is so comparably limited, it is submitted that any alleged conception has no more specificity than simply a wish to know the identity of any material with that requisite biological properties, which can be used to make the claimed compositions and practice the claimed processes, so as to achieve the claimed objectives or effects.

In such instances, the alleged conception fails not merely because the field is unpredictable or because of the general uncertainty surrounding experimental sciences, but because the conception is incomplete due to factual uncertainty that undermines the specificity of the inventor's idea of the invention. *Burroughs Wellcome Co. v. Barr Laboratories Inc.*, 40 F.3d 1223, 1229, 32 USPQ2d 1915, 1920 (Fed. Cir. 1994). Reduction to practice in effect provides the only evidence to corroborate conception (and therefore possession) of the invention.

Lastly, since the claims are not necessarily limited to known materials having the properties of the "maturation agent", but rather to such material that might be identified, given the bid set forth in the instant disclosure to do so, it is noted that one cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483 (Bd. Pat. App. & Int. 1993).

Thus, it is submitted that the instant claims, and the disclosure describing the claimed subject matter, fails to satisfy the written description requirement set forth under 35 U.S.C. § 112, first paragraph.

13. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** a composition comprising a population of isolated dendritic cells prepared *in vitro* by culturing monocytic precursor cells in the presence of human serum albumin and GM-CSF, thereby producing immature dendritic cells, and culturing said immature dendritic cells in the presence of R848, a combination of Bacillus Calmette-Guerin (BCG) and interferon γ (IN$F\gamma$), or a

combination of R848, BCG and INFγ, **and while being enabling for using** a process for promoting an anti-tumor immune response in an individual bearing a tumor comprising administering said composition intratumorally to said tumor in said individual, **as well as being enabling for making and using** any embodiment of the claimed invention that is taught by the prior art, **does not reasonably provide enablement for making and using** the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

M.P.E.P. § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the

claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

The claims are directed to a composition comprising "partially matured dendritic cells" or to a process of using such a composition to produce an anti-tumor immune response.

As explained in the above rejection of the claims under 35 U.S.C. § 112, second paragraph, as well as the rejection of the claims, as failing to meet the written description requirement, the particular features that characterize the claimed "partially matured dendritic cells", which might permit the skilled artisan to immediately envision, recognize or isolate such cells, so as to make and/or use the claimed invention without undue and/or unreasonable experimentation, are not claimed and/or are not clearly (and without ambiguity) described in this application.

Moreover, as explained in the above rejection of the claims, as failing to satisfy the written description requirement, there is no language that adequately describes with the requisite clarity and particularity the claimed "partially matured dendritic cells", which must be used to make and/or use the claimed invention so as to achieve the claimed objectives. Although the claimed cells must be effective to produce an anti-tumor immune response in an individual, a description of what a material does, rather than of what it is, does not suffice to describe the claimed invention. It follows that the claimed invention cannot be made and/or used without the need to first perform undue and unreasonable experimentation.

Then, as also discussed in the above rejection of the claims, as failing to satisfy the written description requirement, the specification discloses that the characteristics of the claimed "partially matured dendritic cells" can vary rather substantially depending upon their origin and the maturation agent that is used to initiate their maturation. Thus, the specification supports the position taken here in that the claims fail to reasonably correspond to the subject matter that is described with due clarity and particularity by the disclosure, so as to satisfy the written description requirement set forth under 35 U.S.C. § 112, first paragraph. This is because it cannot be ascertained whether or not any given dendritic cell should be considered "partially matured" because the features

that characterize such cells are not described in this application with any of the requisite clarity and particularity necessary to permit the skilled artisan to know or determine the identity of the cells; and it follows then that the specification is not reasonable enabling of the production and use of the claimed invention, as it would not be possible to practice the claimed invention without undue and/or unreasonable experimentation.

Turning to a different issue, it is noted that although claims 14-18 are not drawn to a process wherein the dendritic cells are administered directly into the tumor, so as to produce an anti-tumor immune response in the individual, the only process that is exemplified in this application is the process wherein the dendritic cells are administered directly into the tumor[6]. It makes sense that the dendritic cells when administered directly into the tumor might be exposed to tumor antigens, so as to be expected to take up and process those antigens, so as to be capable of eliciting an anti-tumor immune response by, for example, stimulating the activation of tumor antigen-specific cytotoxic T cells. Yet, according to claim 15, for example, the clamed process comprises administering the dendritic cells, not directly into the tumor, but into a tissue area surrounding the tumor; and in such an instance, it is submitted that there is no reason to presume that the dendritic cells, which were injected not into the tumor but into a tissue area surrounding the tumor, will be exposed to tumor antigens, such that it might be expected that the dendritic cells will be capable of eliciting an anti-tumor immune response. Absent some showing of factual evidence or exemplification of such processes then it is submitted that the claimed invention cannot be used to achieve the claimed objective without undue and unreasonable experimentation, particularly since the dendritic cells are not first loaded with peptides derived from the antigens associated with the tumor in the individual. It seems just as likely that naive dendritic cells injected not into the tumor but into a tissue area surrounding the tumor might not elicit an immune response against the tumor. Not dissimilarly, while it might be more probable that naive dendritic cells administered to a lymph node draining a tumor area might be exposed to tumor antigen, it seems one would not should not presume that

[6] See Examples 2-4 at pages 16-19 of the specification.

naïve dendritic cells administered to a circulatory vessel duct that delivers blood or lymph to the area of the tumor will take up and process tumor antigens, so as to elicit an anti-tumor immune response.

Then with regard to claim 18, which is drawn to the method of claim 1, wherein the dendritic cells are administered into the circulatory system "such that the cells are delivered to the cancerous tumor or cancer tumor afflicted organ", the means by which this delivery may occur is apparently left to the reader of the claim. However the need to finish the inventive process by discovering means by which the cells, when administered into the circulatory system, are delivered to the tumor or the organ constitutes a need to first perform undue and unreasonable experimentation before the invention can be used.

Applicant is reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

In deciding *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), the Court indicated the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (CA FC 1997).

In this instance, the overly broad scope of the claims would merely serve as an invitation to one skilled in the art to identify a means by which naïve dendritic cells, when administered into the circulatory system, are delivered to the tumor or the organ, so as to be capable of eliciting an anti-tumor immune response.

Lastly, in light of the fact that the claims are drawn to any of a plurality of materially and structurally disparate compounds that might serve as suitable maturation agents in the practice of the claimed invention, where only a few of such compounds have been described with any of the requisite clarity and particularity and shown to be operable; Applicant is duly reminded that defining a substance by its principal biological

activity amounts to an alleged conception having no more specificity than that of a wish to know the identity of any material with that biological property. See *Colbert v. Lofdahl*, 21 USPQ2d 1068, 1071 (BPAI 1991).

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enabled the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1, 2, 5, 13, 19-23, 25, and 27-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Tanaka et al. (*Gene Therapy*. 2002 Nov; **9**: 1480-1486), as evidenced by Egea et al. (*Expert Rev. Gastroenterol. Hepatol.* 2010 Dec; **4** (6): 723-31).

Tanaka et al. teaches a composition comprising dendritic cells prepared by culturing bone marrow cells in the presence of GM-CSF and IL-4; see entire document (e.g., page 1484, column 2). Tanaka et al. teaches co-administration by intratumoral injection of the dendritic cells in combination with an adenoviral vector encoding IL-18; see, e.g., the abstract. Tanaka et al. teaches the dendritic cells include cells that express increased levels of CD80 and CD86; see, e.g., page 1482, column 1.

As evidenced by Egea et al., GM-CSF is a cytokine that promotes dendritic cell maturation[7].

Although Tanaka et al. describes the dendritic cells as "immature" since the population of cells appears to display a phenotype[8] that is equivalent to that of the "partially matured" dendritic cells described in the specification (Table 2, page 19), absent a showing of any difference, the composition and process disclosed by the prior art are deemed the same as the claimed composition and process.

With regard to claim 19, the specification defines the term "chemotherapy" as inclusive "cytotoxic drugs, apoptotic agents, antibodies, and the like"[9]. Therefore, absent a showing otherwise, the process disclosed by the prior art is deemed the same as the claimed process since the dendritic cells are administered to the individual as an adjuvant to (and in combination with) administration of an adenoviral vector encoding IL-18, a cytokine with potent anti-tumor effects.

For clarity, claim 24 is read as if drawn to a cryopreserved composition and is thus not included in this rejection. Claim 26 is read as if drawn to a composition comprising human dendritic cells, since the cells must express HLA, and is thus not included in this rejection. However, claims 25 and 27-32 are included in this rejection because the claims are drawn to a composition according to claim 21, not processes comprising the active steps recited in these dependent claims. The process steps that may or may not be taken using the claimed composition do not materially or structurally affect the composition and thus the limitations recited in claims 25 and 27-32 are not

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[7] Not inconsistently the specification teaches the same at, e.g., paragraph [0029] of the published application. ("In DCs cultured and partially matured according to the present invention in the presence of a dendritic cell maturation agent, such as GM-CSF and IL-4, the levels of phosphorylated JAK2 (janus activated kinase 2) can be measured to indicate the initiation of maturation by methods well known in the art.)

[8] According toTanaka et al., 85% of the dendritic cells were positive for MHC class II, 81% expressed CD80, 81% expressed CD86, and 68% expressed CD11c (page 1482, column 1). Furthermore, Tanaka et al. teaches the tumor cells killed by IL-18 serve as an antigen source for the dendritic cells to rapidly induce tumor-specific cytotoxic T cells (page 1481, column 2) and since the dendritic cells in combination with the adenoviral vector displayed robust anti-tumor activity it seems apparent that the cells were highly capable of producing an anti-tumor immune response in the individual, which suggest the cells when administered to the individual were capable of taking up and processing antigen *in vivo*; see, e.g., page 1482, column 1.

given weight in discerning any possible differences between the composition disclosed by the prior art and the claimed composition.

16. Claims 1-3, 5, 13, 19-25, and 27-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Garderet et al. (*J. Hematother. Stem Cell Res.* 2001 Aug; **10** (4): 553-67), as evidenced by Egea et al. (*Expert Rev. Gastroenterol. Hepatol.* 2010 Dec; **4** (6): 723-31).

Garderet et al. teaches the production of a composition comprising dendritic cells that have been prepared by culturing monocytes isolated from human blood in the presence of GM-CSF, IL-13, and optionally human serum(autologous or not); see entire document (e.g., the abstract). Garderet et al. teaches the dendritic cells produced in the disclosed manners are capable of taking up and processing antigen; see, e.g., the abstract. Garderet et al. teaches the dendritic cells may be cryopreserved and stored without substantial loss of function or alteration in immunophenotype; see, e.g., the abstract. Garderet et al. teaches the phenotypes of the dendritic cells produced in the disclosed manners roughly correspond to that which defines "immature" dendritic cells in that the cells express CD1a, do not express CD14, and express at most only very low levels of CD83; see, e.g., page 563, column 1. Garderet et al. teaches the dendritic cells produced in the disclosed manners express HLA DR, CD40, CD86, and CD54; see, e.g., page 563, column 1. Garderet et al. teaches the dendritic cells produced in the disclosed manners can be used therapeutically by intratumoral injection, as well as by other delivery routes, depending upon the nature of the dendritic cells and the therapeutic objective; see, e.g., page 563, column 2. For example, Garderet et al. teaches the dendritic cells produced in the disclosed manners can be loaded with tumor antigen before therapeutic use and/or treated so as to undergo maturation; see page 563, column 2. Garderet et al. teaches that mature dendritic cells are thought to be more effect T cell stimulators than immature dendritic cells (page 563, column 2).

[9] See paragraph [0038] of the published application.

As evidenced by Egea et al., GM-CSF is a cytokine that promotes dendritic cell maturation[10].

Although Garderet et al. does not describe any of the preparations of dendritic cells as "partially matured", Garderet et al. describes populations of dendritic cells that appear to display a phenotype[11] that is indistinguishable from (or equivalent to) that of the "partially matured" dendritic cells described in the specification (Table 2, page 19); so therefore, absent a showing of any difference, the composition and process disclosed by the prior art are deemed the same as the claimed composition and process.

For clarity, claims 25 and 27-32 are included in this rejection because the claims are drawn to a composition according to claim 21, not processes comprising the active steps recited in these dependent claims. The process steps that may or may not be taken using the claimed composition do not materially or structurally affect the composition and thus the limitations recited in claims 25 and 27-32 are not given weight in discerning any possible differences between the composition disclosed by the prior art and the claimed composition.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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[10] Not inconsistently the specification teaches the same at, e.g., paragraph [0029] of the published application. ("In DCs cultured and partially matured according to the present invention in the presence of a dendritic cell maturation agent, such as GM-CSF and IL-4, the levels of phosphorylated JAK2 (janus activated kinase 2) can be measured to indicate the initiation of maturation by methods well known in the art.)

[11] According to Garderet et al., the dendritic cells were expressed CD11, CD86 and CD54, for example, and little or no CD83.

18. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. Claims 21 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et al. (*Gene Therapy.* 2002 Nov; **9**: 1480-1486), as evidenced by Egea et al. (*Expert Rev. Gastroenterol. Hepatol.* 2010 Dec; **4** (6): 723-31), in view of Garderet et al. (*J. Hematother. Stem Cell Res.* 2001 Aug; **10** (4): 553-67).

As evidenced by Egea et al., Tanaka et al. teaches that which is set forth in the above rejection of claims 1, 2, 5, 13, 19-23, 25, and 27-32 under 35 U.S.C. § 102(b), but does not expressly teach that the cells can be cryopreserved.

Garderet et al. teaches that dendritic cells can be cryopreserved without causing changes in the immunophenotype of the cells or substantial loss of function; see entire document (e.g., the abstract).

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to have prepared the claimed cyropreserved composition since Garderet et al. teaches that dendritic cells can be cryopreserved without causing changes in the immunophenotype of the cells or substantial loss of function. One ordinarily skilled in the art at the time of the invention would have been motivated to do so to store the composition for later use without causing the cells to undergo changes in immunophenotype or substantial loss of their function.

20. Claims 1, 5, and 6-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et al. (*Gene Therapy.* 2002 Nov; **9**: 1480-1486) or Garderet et al. (*J. Hematother. Stem Cell Res.* 2001 Aug; **10** (4): 553-67), as evidenced by Egea et al.

(*Expert Rev. Gastroenterol. Hepatol.* 2010 Dec; **4** (6): 723-31), in view of Tsuji et al. (*Infect. Immun.* 2000 Dec; **68** (12): 6883-90).

As evidenced by Egea et al., Tanaka et al. teaches that which is set forth in the above rejection of claims 1, 2, 5, 13, 19-23, 25, and 27-32 under 35 U.S.C. § 102(b); and alternatively, as also evidenced by Egea et al., Garderet et al. teaches that which is set forth in the above rejection of claims 1-3, 5, 13, 19-25, and 27-32 under 35 U.S.C. § 102(b).

However, neither Tanaka et al. nor Garderet et al. expressly teaches contacting the dendritic cells with BCG before use or storage.

This deficiency is remedied by the teachings of Tsuji et al., which teaches that dendritic cells treated with whole heat-killed BCG or cell wall skeleton of BCG, for example, initiate a maturation process that produces dendritic cells that more effectively stimulate T cells; see entire document (e.g., the abstract; and page 6887, column 2). Moreover, Tsuji et al. teaches that immature dendritic cells exhibit more potent antigen-presenting ability through uptake of BCG, which serves as an immune potentiator of lymphocytes, or adjuvant, via the maturation of immature dendritic cells; see, e.g., page 6883, column 1, and page 6889. Tsuji et al. teaches that the treatment induces changes in the immunophenotypes of the dendritic cells in that following treatment cells expressed increased levels of CD80 and CD86, for example; see, e.g., page 6885, column 1.

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to have prepared the claimed composition and used it as described by the prior art to stimulate an immune response against a tumor in an individual because Tsuji et al. teaches that dendritic cells treated with whole heat-killed BCG or cell wall skeleton of BCG, for example, initiate a maturation process that produces dendritic cells that more effectively stimulate T cells. One ordinarily skilled in the art at the time of the invention would have been motivated to do so to produce more effective dendritic cells.

Conclusion

21. No claim is allowed.

22. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Kim et al. (*Immunology*. 1999 Aug; **97** (4): 626-633) teaches enhanced antigen-presenting activity and tumour necrosis factor-alpha-independent activation of dendritic cells following treatment with Mycobacterium bovis bacillus Calmette-Guérin. Triolli et al. (*Cancer*. 2000 Dec 15; **89** (12): 2646-54) (of record) teaches intratumoral injection of naive dendritic cells to elicit an anti-tumor immune response in individuals. Mashino et al. (*Mol. Cancer Ther*. 2002 Aug; **1** (10): 785-94) teaches intratumoral injection of naive dendritic cells to elicit an anti-tumor immune response in individuals. Tanaka et al. (*Int. J. Cancer*. 2002 Sep 20; **101** (3): 265-9) teaches intratumoral injection of naive dendritic cells to elicit an anti-tumor immune response in individuals.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHEN RAWLINGS whose telephone number is (571)272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

slr
April 25, 2011